UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,037	04/20/2001	Gordon J. Dow	PU3556USW	9461

23347 7590 01/15/2002

DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY
GLAXOSMITHKLINE
FIVE MOORE DR.
PO BOX 13398
DURHAM, NC 27709-3398

EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	7

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/830,037	Applicant(s) DOW ET AL.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment to claims 1-6, 9, 12-19, 21, and 23-24 submitted October 18, 2001 has been entered and acknowledged.

The outstanding rejection of claims 14, 15, 19, and 23 under 35 USC 112, 2nd paragraph in the previous office action mailed July 18, 2001 has been removed in view of the amendments to the claims.

The outstanding rejection of claims 1, 5, 16, 18, 21, and 22 under 35 USC 102(b) in the previous office action mailed July 18, 2001 has been withdrawn in view of the amendments to the claims. The claims now are directed to the weight percentage of mineral oil or white soft paraffin to be about 2.0 to 5.0%.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 13, 20 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expressions "free of mineral oil or white soft paraffin" and "comprising... about 2.0 to 5.0 wt.% mineral oil or white soft paraffin" in claims 12 and 13 render the claims indefinite because it is unclear whether the fluticasone lotion formulation recited in claims 12 and 13 herein are "free of mineral oil or white soft paraffin" or not. It is confusing.

The expression "chemically and physically stable " in claims 20 and 24 is a relative term which renders the claim indefinite. The expression "chemically and physically stable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The expression renders the claims indefinite as to the degree of stability of the lotion referred to.

Applicant's remarks filed October 18, 2001 regarding the one of ordinary skill would be able to understand what the phrase "chemically and physically stable" means and the instant specification disclosing that the lotion herein is therapeutically stable for at least 6 months at 40°C have been considered but not found persuasive because firstly, the broadest claim herein is not limited by the conditions set forth in the specification: "at least 6 months at 40°C". Secondly, claims 20 and 24 herein recite the limitation "chemically and physically stable for at least 6 months at 40°C" which does not specify the degree of stability of the composition. For example, does the expression "chemically and physically stable" mean a 5% degradation of the composition? Or is a 10%, not 5%, degradation of the composition considered as "chemically and physically stable"? In other words, what degree of resistance to degradation for composition ingredients would render them "chemically and physically stable"? It is not clear what degree of stability encompassed by the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hill (WO 92/14472 from the Information Disclosure Statement received April 20, 2001) and Gordon (Clinical therapeutics, 1998;20(1):26-39) in view of Richards (US Patent 4,985,418), references of rrecord in the previous office action mailed July 18, 2001.

Hill teaches a topical composition employing 0.05% of the corticosteroid, fluticasone propionate, 10.00% of cetostearyl alcohol, 10% of White Soft Paraffin, 2.50% of Polysorbate 60, 10.00% of propylene glycol, and purified water (see particularly Example 1). Hill also teaches that the topical composition is prepared by mixing the ingredients and melting the mixture and then cool the mixture down (See particularly page 2, third paragraph). Hill also teaches that the topical composition is useful in treating skin conditions including inflammation (See particularly page 1, 6th paragraph).

Gordon teaches a corticosteroid containing composition employing Cetostearyl alcohol, cetomacrogol 1000, Isopropyl myristate, propylene glycol. Dimethicone 360, citric acid, sodium citrate, imidurea, and water (see page 28, table 1).

The references do not expressly teach the employment of methyl paraben and propyl paraben in the lotion. The references do not expressly teach the preparation of the topical composition employing mixing the ingredients at an elevated temperature

and then heat the mixture. The references do not expressly teach the viscosity of the topical compositions to be 2,000 to 17,000 cps or 3000 to 13,000 cps. Both references do not expressly teach the blanching score of the lotion. The references do not expressly teach the weight percentage of mineral oil or white soft paraffin to be about 2.0 to 5.0%.

Richards teaches that methyl paraben and propyl paraben are excipients known to be useful in a fluticasone topical composition (See particular col. 5, lines 20-30). Richards also teaches the preparation of the fluticasone composition involving the process of mixing the ingredients at 70 degree Celsius and then heating the mixture to 70 degree (See particular col. 6, line 10-17).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to formulate a topical fluticasone composition with the ingredients herein in the amount herein. It would have also been obvious for one of ordinary skill in the art at the time the invention was made to prepare a topical fluticasone composition that has the viscosity herein and the blanching score herein. It would have also been obvious for one of ordinary skill in the art at the time the invention was made to prepare a topical fluticasone composition by mixing the ingredients at an elevated temperature and then heating up the mixture.

One of ordinary skill in the art would have been motivated to formulate a topical fluticasone composition with the exicipient ingredients in the amount herein because the ingredients herein are known to be useful in formulating topical corticosteroid compositions. Therefore, incorporating all the ingredients herein with any known active

corticosteroid compounds including fluticasone would have been reasonably expected to be useful in preparing the topical corticosteroid composition herein. Furthermore, the optimization of result effect parameters (amount of ingredients such as mineral oil or white paraffin) is obvious as being within the skill of the artisan, absent evidence to the contrary.

One of ordinary skill in the art would have been motivated to prepare a topical fluticasone composition that has the viscosity herein and the blanching score herein because the optimization of result effect parameters (e.g., viscosity and blanching score) is obvious as being within the skill of the artisan, absent evidence to the contrary.

Based on Richards, heating up and mixing the ingredients herein in the method of preparing the topical fluticasone composition is obvious, absent evidence to the contrary.

Applicant's remarks submitted October 18, 2001 regarding the amount of mineral oil or white paraffin encompassed by the amended claims herein have been considered but are believed to be addressed by grounds of rejection above.

It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the

subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In regard to any possible unexpected result presented in the instant application, the specification, the data at pages 14-19 has been considered but not found persuasive as to the presence of unexpected result. The data in page 15, Table 1 demonstrates that the Lotion in Examples 1 and 2 apparently had a higher Area Under the Curve than that of Cutivate® cream. However, it is not clear as to the statistical error of the measurement. Further, it is unclear that Cutivate cream represents the closest prior art for evaluation of unexpected results by comparison. Therefore the data does not clearly and convincingly demonstrate unexpected results. The nature of the composition of Cutivate® cream demonstrated in the specification herein, e.g., ingredients and amount of each is unclear. Therefore, the relevance of the AUC difference in Table 1 determining unexpected results for the claimed invention over the closest prior art is unclear.

In regard to the data in page 16, Table 2, the AUC and the blanching score of the fluticasone lotion within the instant claims is apparently higher than Cutivate cream and Hytone™ lotion but is lower than the Temovate™ and Elocon™. However, the statistical error of the measurement is not presented. Therefore the data does not clearly and convincingly demonstrate unexpected results. Moreover, it is not clear that Cutivate® cream, Hytone lotion, Temovate, and Elocon represent the closest prior art for evaluation of unexpected results by comparison. The nature of the compositions of Cutivate® cream, Hytone lotion, Temovate, Elocon demonstrated in the specification herein, e.g., ingredients and amount of each is unclear. Therefore, the relevance of the

AUC and blanching score difference in Table 2 on page 16 determining unexpected results for the claimed invention over the closest prior art is unclear.

The data presented in Table 3 of page 17 demonstrates the effectiveness of the fluticasone lotion within the claims in treating atopic dermatitis as compared to a placebo. It is seen to be an expected therapeutic result based on the cited prior art. The data in Table 4, page 18-19 demonstrates the safety of the employment of fluticasone lotion. Please note that the use of fluticasone lotion to achieve therapeutic effect is expected to be safe. No comparative data is present to evaluate the unexpected result. Moreover, it is not clear the amount of fluticasone lotion which was applied. It is not clear what the percentage of subjects using Cutivate cream experiencing side effects is. In addition, it is unclear that Cutivate cream represents the closest prior art for evaluation of unexpected results by comparison. Therefore no clear and convincing unexpected results are seen to be present herein.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
January 11, 2002

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600